Serial No. 08/017,931, filed February 12, 1993, abandoned, and is a continuation-in-part of U.S. Application Serial No. 08/292,597, filed August 18, 1994, U.S. Pat. No. 5,834,266 which in turn is a continuation-in-part of U.S. Application Serial No. 08/179,143, filed January 7, 1994, abandoned, which in turn is a continuation-in-part of U.S. Application Serial No. 08/093,499, filed Jul. 16, 1993 abandoned. The contents of each of these applications is hereby incorporated by referenced into the present disclosure. The full contents of related cases PCT/US94/01617, PCT/US94/01660 and PCT/US94/08008 are also incorporated by reference into the present disclosure.

At page 90:

Dimerization and oligomerization of proteins are general biological control mechanisms that contribute to the activation of cell membrane receptors, transcription factors, vesicle fusion proteins, and other classes of intra- and extracellular proteins. We have developed a general procedure for the regulated (inducible) dimerization or oligomerization of intracellular proteins.

~~Dimerization and oligomerization of proteins are general biological control mechanisms that contribute to the activation of cell membrane receptors, transcription factors, vesicle fusion proteins, and other classes of intra- and extracellular proteins. We have developed a general procedure for the regulated (inducible) dimerization or oligomerization of intracellular proteins. In principle, any two target proteins can be induced to associate by treating the cells or organisms that harbor them with cell permeable, synthetic ligands. To illustrate the practice of this invention, we have induced: (1) the intracellular aggregation of the cytoplasmic tail of the ζ chain of the T cell receptor (TCR) CD3 complex thereby leading to signaling and transcription of a reporter gene, (2) the homodimerization of the cytoplasmic tail of the Fas receptor thereby leading to cell-specific apoptosis (programmed cell death) and (3) the heterodimerization of a DNA-binding domain (Gal4) and a transcription-activation domain (VP16) thereby leading to direct transcription of a reporter gene.~~

~~Regulated intracellular protein association with our cell permeable, synthetic ligands offers new capabilities in biological research and medicine, in particular, in gene therapy. Using gene transfer techniques to introduce our artificial receptors, one can turn on or off the signaling pathways that lead to the overexpression of therapeutic proteins by administering orally active "dimerizers" or "de-dimerizers", respectively. Since cells from different recipients can be~~

~~configured to have the pathway overexpress different therapeutic proteins for use in a variety of disorders, the dimerizers have the potential to serve as "universal drugs". They can also be viewed as cell permeable, organic replacements for therapeutic antisense agents or for proteins that would otherwise require intravenous injection or intracellular expression (e.g., the LDL receptor or the CFTR protein).~~

In the claims:

For the convenience of the Examiner, all claims being examined, whether or not amended, are presented below.

Please cancel, without prejudice, claims 1, 6, 20, 21, 31, 36, 37, 38, 39 and 45.

C3

14. **(Twice Amended)** A vector including a DNA construct of claim 22 and a selectable marker permitting transfection of the DNA construct into host cells and selection of transfectants containing the construct.

C4

18. **(Amended)** A mammalian cell which contains and expresses at least one nucleic acid construct of claim 22, 23, or 49.

C5

22. **(Amended)** A nucleic acid composition comprising at least two genetic constructs, each encoding a chimeric protein,

(a) a first construct encoding a first chimeric protein comprising at least one ligand-binding domain and a transcriptional activation domain which is heterologous thereto,

(b) a second construct encoding a second chimeric protein comprising at least one ligand-binding domain which may be the same or different from a ligand binding domain of the first chimeric protein, and a DNA binding domain,

wherein the first and second of said chimeric proteins together (i) bind to a ligand to form a ligand cross-linked protein complex, and (ii) in a ligand dependent manner, activate